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☐ 1: [P29473](#). Reports Nitric-oxide synt...[gi:266647]

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LOCUS P29473 1205 aa linear MAM 20-FEB-2007
DEFINITION Nitric-oxide synthase, endothelial (EC-NOS) (NOS type III) (NOSIII) (Endothelial NOS) (eNOS) (Constitutive NOS) (cNOS).
ACCESSION P29473
VERSION P29473 GI:266647
DBSOURCE swissprot: locus NOS3_BOVIN, accession [P29473](#);
 class: standard.
 created: Apr 1, 1993.
 sequence updated: Jan 23, 2007.
 annotation updated: Feb 20, 2007.
 xrefs: [M99057.1](#), [AAA30667.1](#), [M89952.1](#), [AAA30494.1](#), [M95674.1](#),
[AAA30669.1](#), [A38943](#), [1D0CA](#), [1D0CB](#), [1D0OA](#), [1D0OB](#), [1D1VA](#), [1D1VB](#),
[1D1WA](#), [1D1WB](#), [1D1XA](#), [1D1XB](#), [1D1YA](#), [1D1YB](#), [1DM6A](#), [1DM6B](#), [1DM7A](#),
[1DM7B](#), [1DM8A](#), [1DM8B](#), [1DMIA](#), [1DMIB](#), [1DMJA](#), [1DMJB](#), [1DMKA](#), [1DMKB](#),
[1ED4A](#), [1ED4B](#), [1ED5A](#), [1ED5B](#), [1ED6A](#), [1ED6B](#), [1FOIA](#), [1FOIB](#), [1FOJA](#),
[1FOJB](#), [1FOLA](#), [1FOLB](#), [1FOOA](#), [1FOOB](#), [1FOPA](#), [1FOPB](#), [1I83A](#), [1I83B](#),
[1NSEA](#), [1NSEB](#), [1P6LA](#), [1P6LB](#), [1P6MA](#), [1P6MB](#), [1P6NA](#), [1P6NB](#), [1Q2OA](#),
[1Q2OB](#), [1RS8A](#), [1RS8B](#), [1RS9A](#), [1RS9B](#), [1ZZSA](#), [1ZZSB](#), [1ZZTA](#), [1ZZTB](#),
[2NSEA](#), [2NSEB](#), [3NSEA](#), [3NSEB](#), [4NSEA](#), [4NSEB](#), [5NSEA](#), [5NSEB](#), [6NSEA](#),
[6NSEB](#), [7NSEA](#), [7NSEB](#), [8NSEA](#), [8NSEB](#), [9NSEA](#), [9NSEB](#)
 xrefs (non-sequence databases): UniGene:Bt.4662, KEGG:bta:287024,
 LinkHub:P29473, InterPro:IPR003097, InterPro:IPR001094,
 InterPro:IPR008254, InterPro:IPR001709, InterPro:IPR004030,
 InterPro:IPR012144, InterPro:IPR001433, Pfam:PF00667, Pfam:PF00258,
 Pfam:PF00175, Pfam:PF02898, PIRSF:PIRSF000333, PRINTS:PR00369,
 PRINTS:PR00371, PROSITE:PS50902, PROSITE:PS60001
KEYWORDS 3D-structure; Blood coagulation; Calcium; Calmodulin-binding; FAD;
 FMN; Heme; Iron; Lipoprotein; Metal-binding; Myristate; NADP;
 Oxidoreductase; Palmitate; Phosphorylation; Zinc.
SOURCE Bos taurus (cattle)
ORGANISM Bos taurus
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Laurasiatheria; Cetartiodactyla; Ruminantia;
 Pecora; Bovidae; Bovinae; Bos.
REFERENCE 1 (residues 1 to 1205)
AUTHORS Lamas,S., Marsden,P.A., Li,G.K., Tempst,P. and Michel,T.
TITLE Endothelial nitric oxide synthase: molecular cloning and
 characterization of a distinct constitutive enzyme isoform
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 89 (14), 6348-6352 (1992)
PUBMED [1378626](#)
REMARK NUCLEOTIDE SEQUENCE [MRNA].
REFERENCE 2 (residues 1 to 1205)

AUTHORS Nishida,K., Harrison,D.G., Navas,J.P., Fisher,A.A., Dockery,S.P.,
Uematsu,M., Nerem,R.M., Alexander,R.W. and Murphy,T.J.

TITLE Molecular cloning and characterization of the constitutive bovine
aortic endothelial cell nitric oxide synthase

JOURNAL J. Clin. Invest. 90 (5), 2092-2096 (1992)

PUBMED [1385480](#)

REMARK NUCLEOTIDE SEQUENCE [MRNA].

REFERENCE 3 (residues 1 to 1205)

AUTHORS Sessa,W.C., Harrison,J.K., Barber,C.M., Zeng,D., Durieux,M.E.,
D'Angelo,D.D., Lynch,K.R. and Peach,M.J.

TITLE Molecular cloning and expression of a cDNA encoding endothelial
cell nitric oxide synthase

JOURNAL J. Biol. Chem. 267 (22), 15274-15276 (1992)

PUBMED [1379225](#)

REMARK NUCLEOTIDE SEQUENCE [MRNA].
TISSUE=Aortic endothelium

REFERENCE 4 (residues 1 to 1205)

AUTHORS Busconi,L. and Michel,T.

TITLE Endothelial nitric oxide synthase. N-terminal myristoylation
determines subcellular localization

JOURNAL J. Biol. Chem. 268 (12), 8410-8413 (1993)

PUBMED [7682550](#)

REMARK MYRISTOYLATION AT GLY-2.

REFERENCE 5 (residues 1 to 1205)

AUTHORS Robinson,L.J. and Michel,T.

TITLE Mutagenesis of palmitoylation sites in endothelial nitric oxide
synthase identifies a novel motif for dual acylation and
subcellular targeting

JOURNAL Proc. Natl. Acad. Sci. U.S.A. 92 (25), 11776-11780 (1995)

PUBMED [8524847](#)

REMARK PALMITOYLATION AT CYS-15 AND CYS-26.

REFERENCE 6 (residues 1 to 1205)

AUTHORS Boo,Y.C., Hwang,J., Sykes,M., Michell,B.J., Kemp,B.E., Lum,H. and
Jo,H.

TITLE Shear stress stimulates phosphorylation of eNOS at Ser(635) by a
protein kinase A-dependent mechanism

JOURNAL Am. J. Physiol. 283, H1819-H1828 (2002)

PUBMED [12384459](#)

REMARK PHOSPHORYLATION AT THR-497; SER-635 AND SER-1179.

REFERENCE 7 (residues 1 to 1205)

AUTHORS Raman,C.S., Li,H., Martasek,P., Kral,V., Masters,B.S. and
Poulos,T.L.

TITLE Crystal structure of constitutive endothelial nitric oxide
synthase: a paradigm for pterin function involving a novel metal
center

JOURNAL Cell 95 (7), 939-950 (1998)

PUBMED [9875848](#)

REMARK X-RAY CRYSTALLOGRAPHY (1.9 ANGSTROMS) OF 67-482.

REFERENCE 8 (residues 1 to 1205)

AUTHORS Li,H., Raman,C.S., Martasek,P., Kral,V., Masters,B.S. and
Poulos,T.L.

TITLE Mapping the active site polarity in structures of endothelial
nitric oxide synthase heme domain complexed with isothioureas

JOURNAL J. Inorg. Biochem. 81 (3), 133-139 (2000)

PUBMED [11051558](#)

REMARK X-RAY CRYSTALLOGRAPHY (1.86 ANGSTROMS) OF 67-482.

REFERENCE 9 (residues 1 to 1205)

AUTHORS Li,H., Raman,C.S., Martasek,P., Masters,B.S. and Poulos,T.L.

TITLE Crystallographic studies on endothelial nitric oxide synthase
complexed with nitric oxide and mechanism-based inhibitors

JOURNAL Biochemistry 40 (18), 5399-5406 (2001)
 PUBMED [11331003](#)
 REMARK X-RAY CRYSTALLOGRAPHY (1.93 ANGSTROMS).
 REFERENCE 10 (residues 1 to 1205)
 AUTHORS Raman,C.S., Li,H., Martasek,P., Southan,G., Masters,B.S. and Poulos,T.L.
 TITLE Crystal structure of nitric oxide synthase bound to nitro indazole reveals a novel inactivation mechanism
 JOURNAL Biochemistry 40 (45), 13448-13455 (2001)
 PUBMED [11695891](#)
 REMARK X-RAY CRYSTALLOGRAPHY (1.65 ANGSTROMS).
 REFERENCE 11 (residues 1 to 1205)
 AUTHORS Raman,C.S., Li,H., Martasek,P., Babu,B.R., Griffith,O.W., Masters,B.S. and Poulos,T.L.
 TITLE Implications for isoform-selective inhibitor design derived from the binding mode of bulky isothioureas to the heme domain of endothelial nitric-oxide synthase
 JOURNAL J. Biol. Chem. 276 (28), 26486-26491 (2001)
 PUBMED [11331290](#)
 REMARK X-RAY CRYSTALLOGRAPHY (1.93 ANGSTROMS).
 REFERENCE 12 (residues 1 to 1205)
 AUTHORS Kotsonis,P., Frohlich,L.G., Raman,C.S., Li,H., Berg,M., Gerwig,R., Groehn,V., Kang,Y., Al-Masoudi,N., Taghavi-Moghadam,S., Mohr,D., Munch,U., Schnabel,J., Martasek,P., Masters,B.S., Strobel,H., Poulos,T., Matter,H., Pfeleiderer,W. and Schmidt,H.H.
 TITLE Structural basis for pterin antagonism in nitric-oxide synthase. Development of novel 4-oxo-pteridine antagonists of (6R)-5,6,7,8-tetrahydrobiopterin
 JOURNAL J. Biol. Chem. 276 (52), 49133-49141 (2001)
 PUBMED [11590164](#)
 REMARK X-RAY CRYSTALLOGRAPHY (2.35 ANGSTROMS).
 COMMENT On Mar 15, 2005 this sequence version replaced [gi:1083055](#).
 [FUNCTION] Produces nitric oxide (NO) which is implicated in vascular smooth muscle relaxation through a cGMP-mediated signal transduction pathway. No mediates vascular endothelial growth factor (VEGF)-induced angiogenesis in coronary vessels and promotes blood clotting through the activation of platelets.
 [CATALYTIC ACTIVITY] L-arginine + n NADPH + m O(2) = citrulline + nitric oxide + n NADP(+).
 [COFACTOR] Heme group.
 [COFACTOR] Binds 1 FAD.
 [COFACTOR] Binds 1 FMN.
 [COFACTOR] Metrahydrobiopterin (BH4). May stabilize the dimeric form of the enzyme.
 [ENZYME REGULATION] Stimulated by calcium/calmodulin.
 [SUBUNIT] Homodimer.
 [SIMILARITY] Belongs to the NOS family.
 [SIMILARITY] Contains 1 flavodoxin-like domain.
 FEATURES Location/Qualifiers
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 Protein 1..1205
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 /EC_number="1.14.13.39"
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Region 103..104
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Region 165
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Region 447..450
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Region 455
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Region 459
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Region /gene="NOS3"
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492..512

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/note="Calmodulin-binding (Potential)."
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/note="Phosphothreonine (by PKA)."
514..1162

Region /gene="NOS3"
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522..705

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/site_type="np-binding"
/inference="non-experimental evidence, no additional details recorded"
/note="FMN (By similarity)."
741

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Region 907..908
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Site 937..947
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/note="FAD (By similarity)."
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Site 1012..1030
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/note="NADP (By similarity)."
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/experiment="experimental evidence, no additional details recorded"
/note="A -> H (in Ref. 3)."
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/note="Phosphoserine (by PDPK1 and PKA)."

ORIGIN

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121 paeqlqsar  dfinqyyssi  krsqsqahee  rlqeveaeva  stgtyhlres  elvfgakqaw
181 rnaprcvgri  qwgklqvfa  rdcssaquemf  tyicnhikya  tnrgnlrsai  tvfpqrapgr
241 gdfriwnsql  vryagyrqqd  gsvrgdpanv  eitelciqhg  wtpgngrfdv  lp111lapde
301 apelfvlppe  lvlevplehp  tlewfaalgl  rwyalpavsn  m1leigglef  saapfsgwym
361 steigtrnlc  dphryniled  vavcmdldtr  ttsslwkdk  aveinlavlh  sfqlakvtiv
421 dhhaatvsfm  khldneqkar  ggcpadwawi  vppisgsltp  vfhqemvnyi  lspafryqpd
481 pwkgsatkga  gitrkktfke  vanavkisas  lmgtlmakrv  katilyaset  graqsyaqql
541 grlfrkafdp  rvlcmdeydv  vslehealvl  vvtstfgngd  ppengesfaa  almmsgpyn
601 ssprpeqhks  ykirfnsvsc  sdplvsswrr  krkessntds  agalg1trfc  vfglgsrayp
661 hfcafaravd  trleelgger  llqlgqgdel  cgqeeafrgw  akaafgasce  t1cvgeeaka
721 aaqdifspkr  swkrqyr1ls  tqaeglql1p  glihvhrkm  fqatvlsven  lqsskstrat
781 ilvrl1tagq  eglqyqp1gdh  igicppnrpg  lveallsrve  dppp1tesva  veqlekgspg
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961 vlayrtq1dgl  gplhygv1cst  wlsqlktgdp  vpcfirgaps  fr1ppdp1yp  cilvgp1gtgi
1021 apfrgfwqer  lhdieskg1lq  papmtlvf1gc  rcsqldh1lyr  devqdaqerg  vfgrv1tafs
1081 repdspktyv  qd1ilrtelaa  evhrvlcler  ghmfvcg1dvt  mat1svlqtvq  rilategdme
1141 ldeagdvigv  lrdqqr1yhed  ifgl1tlrtqe  vtsrirtqsf  slqerh1lrga  vpwa1fdppgp
1201 dtpgp
```

//

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